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Contact Details

Histocompatibility and Immunogenetics Laboratory,
Scottish National Blood Transfusion Service,
Royal Infirmary of Edinburgh,
51 Little France Crescent,
Edinburgh,
EH16 4SA
Tel: 0131-242-7528, Fax: 0131-242-7530

Consultant Clinical Scientists (Histocompatibility & Immunogenetics)
Dr David Turner (Consultant Clinical Scientist)
Tel: 0131-242-7534
Email: david.turner2@nhs.net

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Email: Richard.battle@nhs.net

Consultant Haematologists
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Tel: 0131-242-7527
Email: lynn.manson@nhs.net

Dr Megan Rowley
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Email: megan.rowley@nhs.net

H&I Laboratory Manager
Sylvia McConnell
Tel: 0131-242-7518
Email: sylvia.mcconnell@nhs.net

H&I Senior Laboratory Staff
Tel: 0131-242-7528
Email: NSS.handi@nhs.net

Out of Hours Requests: (A Clinical Scientist is also available 24/7 for clinical advice relating to any results generated within the H&I laboratory).

Solid Organ: There is an on-call healthcare scientist for solid organ transplant related work. It is the transplant co-ordinator/ Clinical Scientist’s responsibility to initiate call out.
Aims of the Laboratory

1. To provide a comprehensive histocompatibility service to support the East of Scotland Transplant Unit.

2. To provide a comprehensive platelet immunohaematology service to support patients who are refractory to platelet transfusions and suspected cases of neonatal alloimmune thrombocytopenia.

3. To provide a service for CD34+ stem cell enumeration to support stem cell collection and processing within SNBTS.

4. To provide an HLA typing service to aid in the diagnosis of various disorders.

5. To maintain and improve the service in response to our users' needs.

Complaints/ Comments/ Suggestions
SNBTS as a Strategic business Unit (SBU) of NSS is committed to capturing and recording feedback from service users and reviewing this correspondence as part of its Continual Improvement Programme. In the event that a user is dissatisfied with any aspect of the service they have received, then they are encouraged to contact any of the addressees identified in the contacts section (page 3) to discuss their concerns.

Protection of Personal Information
In line with National Services Scotland (NSS) Information Security policies the laboratory has in place information technological and organisational safeguards to ensure that the confidentiality, integrity and availability of all forms of information held on patients, donors, NHSScotland staff and family health contractors, it is not lost or compromised.

Quality Assurance
A Quality Management System monitors and audits all aspects of the service. All laboratory investigations and clerical procedures are governed and maintained by compliance with the SEBTS Quality Manual, Management Procedures and relevant Standard Operating Procedures (SOPs).
Standards of testing are maintained by the rigorous use of internal quality assurance protocols and through participation in appropriate external quality assessment schemes (UK NEQAS).

Quality Assessment and External Audit

A copy of last year’s participation certificate and results summary is available, on request, for each of the following:

- **UK NEQAS for Histocompatibility and Immunogenetics**
- **UK NEQAS for Leucocyte Immunophenotyping (for CD34 enumeration testing)**

**Accreditation**

The Edinburgh H&I laboratory is accredited through United Kingdom Accreditation Service (UKAS) and the European Federation for Immunogenetics (EFI).

**Human Tissue Act (Scotland) 2006**

From April 2007 the laboratory has been in compliance with the Human Tissue Act (Scotland) 2006.
General Laboratory Information

Laboratory hours

Routine    Monday to Friday        08.30 to 17.00.

Last receipt for samples is 17.00 on Friday.

Please note that each request accepted by the laboratory for examination(s) shall be considered an agreement.

Sample Labelling

Samples that are received for laboratory examinations must be labelled in accordance with the SNBTS Policy on The acceptance criteria for sample labelling within clinical laboratories (detailed on page 7). All samples must be labelled with the patient’s CHI number – an alternative unique identifier (hospital number or emergency number) may only be used if the patient does not yet have a CHI number. If addressograph labels are used for sample request forms and/or sample tubes the responsibility is with the clinician/responsible person taking the sample. Samples received that do not meet with the described sample acceptance criteria may not be tested.
Please note addressograph labels are NOT acceptable on SAMPLE TUBES for transfusion related work

Sample Tubes – ideally need to be hand written CLEARLY, although addressograph labels are acceptable for non-transfusion related work

SNBTS Policy on the Acceptance Criteria for Patient Blood Samples within Clinical Laboratories

<table>
<thead>
<tr>
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<th>Requirement</th>
<th>Consequence if missing from sample tube</th>
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</thead>
<tbody>
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<td>Mandatory</td>
<td>Discard</td>
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<tr>
<td>Forename (correctly spell in full)</td>
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<td>Unique Identification number*</td>
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<th>Requirement</th>
<th>Consequence if missing from request form</th>
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<tbody>
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<td>Discard</td>
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<tr>
<td>Unique Identification number*</td>
<td></td>
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</tr>
</tbody>
</table>

* Clinical details for request e.g. pre-PRT, rejection, Bipap, etc.

<table>
<thead>
<tr>
<th>Details of referring clinician (location of patient area/destination of report)</th>
<th>Desirable</th>
<th>Requestor may be contacted to discuss request**</th>
</tr>
</thead>
</table>

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* All samples must be labelled with the patient’s CHI number – an alternative unique identifier (hospital number or emergency number) may be used if the patient does not have a CHI number.

** Requestor is responsible for ensuring the H&I laboratory is made aware of any special requirements that may be necessary.
Sample Factors Influencing Test Performance and Results

Haemolysed samples may influence test results and receipt of a haemolysed sample may result in the request for a replacement. All serological tests require fresh samples that have been bled in the last 48 hours.

Certain immunosuppressive agents may influence the tests undertaken in H&I. These include, ATG, IvIg and monoclonal antibodies therapies including Rituximab. If patients are known to be receiving these agents, this should be highlighted to the laboratory on the request form.

DNA typing of haematology patients may prove difficult if the patient is pancytopenic and therefore efforts should be made to HLA type patients early on in their treatment.

Transfer of samples via SNBTS/ LUHT Transport

Samples that originate from the Grampian and Tayside areas are transported to the Edinburgh H&I laboratory by SNBTS scheduled runs. It is the responsibility of the clinical team to ensure that any samples for transfer to Edinburgh reach the required dispatch area of local blood banks. Samples should be placed in red clinical transportation box by SNBTS staff for delivery.

Samples from Lothian hospitals and Lothian GP practices are uplifted by the LUHT van service.

Sample Referrals

Samples for HPA and HNA testing are referred to:

NHS Blood and Transplant
500 North Bristol Park
Filton
Bristol
BS34 7QH

Exact sample requirements should be discussed with the H&I laboratory.
Requirements for sending samples by Royal Mail

Samples must be packaged in accordance with Packaging Instruction P650 (UN3373, Diagnostic Specimens). Briefly this state:

The packaging shall consist of three components:

a) A primary receptacle
b) A secondary packaging
c) An outer packing

Primary receptacles shall be packed in secondary packaging in such a way that, under normal conditions of carriage, they cannot break, be punctured or leak their contents into the secondary packaging. Secondary packaging shall be secured in outer packaging with suitable cushioning material. Any leakage of the contents shall not compromise the integrity of the cushioning material or of the outer packaging. For carriage, the mark illustrated below shall be displayed on the external surface of the outer packaging on a background of a contrasting colour and shall be clearly visible and legible. The width of the line shall be at least 2mm; the letters and numbers shall be at least 6mm high.

UN 3373
**Reporting Times**

The laboratory aims to meet the following targets in reporting results.

Any urgent requests should be discussed with the laboratory, particularly post transplant antibody monitoring samples.

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<th>Time</th>
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<tbody>
<tr>
<td>HLA Type</td>
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<tr>
<td>Post transplant antibody monitoring</td>
<td>2 days</td>
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<td>HLA Type of local donor</td>
<td>5 hours</td>
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<tr>
<td>Crossmatch result</td>
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<td>(Renal cadaver donor, from receipt of tissue samples)</td>
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<td>(Living Renal Donor)</td>
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</tr>
<tr>
<td>Disease Association testing</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Platelet testing</td>
<td>2 days</td>
</tr>
<tr>
<td>CD34 enumeration</td>
<td>&lt; 2hrs</td>
</tr>
<tr>
<td>MAIPA &amp; HNA testing (tested by NHSBT Bristol)</td>
<td>2 weeks</td>
</tr>
</tbody>
</table>
Section I

Histocompatibility Testing for Solid Organ Transplantation

H&I services are provided for the renal, SPK, islet and liver transplant units.

Potential kidney, pancreas and islet transplant recipients, local multi-organ deceased donors, deceased donors referred from NHSBT Organ Donation and Transplant (ODT) and potential living donors are HLA typed. HLA typing is performed by PCR based assays.

Crossmatching for living or deceased donor transplants is performed by flow cytometry.

HLA antibody screening is performed by Luminex technology, which is a bead based immunoassay used to semi quantitatively detect HLA IgG antibodies.

Kidney, Kidney/Pancreas, Kidney/Islet and Islet Transplant Patients

New patients have a full HLA type and antibody screen. Samples required are:

- **5ml EDTA** for HLA class I & II typing
- **10ml Clotted Sample** for HLA antibody screening

Prior to listing on the transplant waiting list a confirmatory HLA type needs to be performed as well as an up to date antibody screen. Samples required are:

- **5ml EDTA** for HLA class I & II typing
- **10ml Clotted Sample** for HLA antibody screening

When the confirmatory type and antibody screen have been completed and the transplant co-ordinators request that the patient is listed, the laboratory will enter information into the ODT NTxD website. Once active on the Waiting List, a **10ml clotted sample** should be sent to the laboratory every 3 months. The serum is screened for HLA antibodies and stored for use in future crossmatches.
Liver Patients

Patients are not HLA typed prior to transplant. At the time of transplant the following sample should be provided to the H&I lab:

10ml Clotted Sample for archiving

Potential Deceased donor

The Specialist Nurse for Organ Donation will liaise with the laboratory, or if out of hours the on-call Healthcare Scientist, when a potential deceased donor is identified.

The H&I lab will HLA type potential donors. Results are then emailed to NHSBT ODT for organ allocation.

An HLA antibody investigation or flow crossmatch may be performed using current serum samples and donor lymphocytes, to aid in the interpretation of the risks involved.

Donor: Tissue Samples/EDTA
Recipient: 10 ml clotted and 10ml EDTA pre-transplant sample

Imported Deceased Donor

The renal transplant coordinator will liaise with the laboratory, or if out of hours, the on-call Consultant Clinical Scientist, when NHSBT ODT allocates a kidney, pancreas, or islets to a patient on the local waiting list.

Samples required are:

Donor: Tissue Samples
Recipient: 10 ml clotted and 10ml EDTA pre-transplant sample

Virtual Crossmatching

A virtual crossmatch eliminates the need for a prospective crossmatch and benefits the patient by reducing the cold ischaemic time of the graft. For kidney, kidney/pancreas, kidney/islet and islet cases, patients may be eligible for a virtual crossmatch if:
1) they have not received a previous graft
2) they have been shown to be consistently negative for HLA antibodies by Luminex testing or have a consistent HLA antibody profile
3) they have sent a recent (<3 months) sample to the laboratory and have had no sensitising events since the last sample was tested i.e. transfusions, failed pregnancies etc

The recipient transplant coordinator will hold a list of these patients and they will confirm with the Consultant Clinical Scientist that a pre-transplant crossmatch is not necessary.

**Donor and recipient samples are still required to be sent to the lab.**

**Reporting of Crossmatch Results**

Results of the compatibility testing will be phoned to the recipient transplant co-ordinator as soon as they are available. A report of the crossmatch results will be generated and emailed to the recipient transplant co-ordinator. Reports will show the flow crossmatch results and may include a comment to aid interpretation of the data generated. Any unexpected positive crossmatch results will be discussed between the on call Healthcare Scientist and the on call Consultant Clinical Scientist who will also be available to discuss any findings with the clinical team. Please be aware that as the data generated by the flow cytometer is numerical and semi-quantitative, there is an inherent uncertainty (or variability) in the data generated. The lab has carried out appropriate testing in line with the ‘Recommendations for the determination of measurement uncertainty for assays performed in the histocompatibility and immunogenetics (H&I) laboratory’, 2016, to estimate the variability of this assay using statistical analysis. Please contact the laboratory for discussion or advice on results if necessary.
Living Donor Transplants (local, altruistic or paired exchange)

If a potential living donor has been identified for a patient then an initial (virtual) crossmatch must be performed.

Samples required for initial (virtual) testing are:

- **Donor**: 10ml EDTA or Sodium Citrate for initial compatibility assessment
- **Recipient**: 10ml Clotted Sample for HLA antibody screening
  10ml EDTA for HLA class I & II typing

A final ‘wet’ crossmatch must be performed prior to the planned operation.

Samples required for the final ‘wet crossmatch are:

- **Donor**: 40ml EDTA or Sodium Citrate
- **Recipient**: 10ml Clotted Sample for HLA antibody screening
  40ml EDTA for auto crossmatch

Post Transplant Monitoring

Post solid organ transplant samples will only be screened for HLA antibodies if clinically indicated, i.e. patients creatinine has risen and /or there is evidence of biopsy proven rejection. It is therefore important that the request form accompanying these samples indicates that these conditions exist for the test to be performed.
Section II

CD34+ Stem Cell Enumeration Testing of Autologous Haematopoietic Stem Cell Transplant Patients

The laboratory provides flow cytometric enumeration of CD34+ hematopoietic stem and progenitor cells (HSCs) for evaluation of graft adequacy of peripheral blood and bone marrow stem cell grafts.

Samples are provided by the Clinical Apheresis Unit (CAU) and Tissues, Cells and Advanced Therapeutics (TCAT) for evaluation.

Please be aware that as the CD34 enumeration assay gives an absolute value, there is an inherent uncertainty (or variability) in the data generated. Testing of high and low control samples in the CD34 enumeration assay enables an assessment of this uncertainty of measurement. Please contact the laboratory for discussion or advice on results if necessary.
Section III

Platelet Immunohaematology

The H&I laboratory provides both platelet antibody screening and platelet antigen typing to aid in the investigation, diagnosis and possible treatment of a variety of thrombocytopenias.

Platelet investigations are undertaken in cases of immunological platelet refractoriness and suspected cases of foetal neonatal alloimmune thrombocytopenia (FNAIT).

Any request for platelet investigations should be discussed with the BTS/Haematology duty specialist registrar. The duty specialist registrar can be contacted by phoning the laboratory and giving the patient’s details, the requesting doctor’s name and phone number, so that the duty specialist registrar can phone them or by contacting the switchboard at the RIE directly on 0131 242-1000 and asking for the ‘duty BTS registrar’.

Foetal Neonatal Alloimmune Thrombocytopenia (FNAIT)

FNAIT is caused by maternal IgG alloantibodies directed against HPA present in the fetus/neonate and absent in the mother. Whilst numerous alloantigens have been described, HPA-1a is the most immunogenic and accounts for approximately 80% of severe cases. The next most common is HPA-5b.

Investigation of FNAIT will be undertaken after the requesting doctor discusses the case with the BTS/Haematology duty specialist registrar. Initial platelet antibody screening will be performed on a Luminex platform using the PAK-LX assay.

If specific platelet antibodies are found the parents/baby can be HPA typed and the phenotype of mother and father/baby compared. This will help to identify any HPA antigens to which the mother might have developed antibodies.
Samples Required:  

- **10mls Clotted and 5ml EDTA** from mum for HPA screening and HPA typing  
- **5ml EDTA** from dad for HPA typing  
- **1ml EDTA** from baby for HPA typing  

**HLA/HPA Matched Platelets for Platelet Refractoriness**

Platelet Transfusion Refractoriness may result from immune or non-immune platelet destruction. The following can be targets for clinically relevant platelet allo-antibodies that can cause immune platelet refractoriness.

1. the ABO blood system  
2. HLA class I antigens.  
3. Human Platelet Antigens (HPA)

The H&I Laboratory investigates the presence of allo-antibodies against HLA class I antigens and/or antibodies directed against HPA. It should be noted that HPA antibodies in the absence of HLA class I antibodies are a rare cause of poor increments. The exception is if the HPA antibody is against a high frequency HPA alloantigens (e.g. HPA-1a) when it might cause poor increments with platelets from nearly all random donors.

Samples Required:  

- **10ml Clotted Sample** for HLA/HPA antibody screen  
- **5ml EDTA** for HLA/HPA typing

Depending on the antibody and typing results, HLA class I and/or HPA compatible platelets can be provided.

For the provision of HLA/HPA matched platelets the following criteria should be met:

1. Exclusion of non-immune causes of platelet refractoriness  
2. Platelet refractoriness to ABO compatible platelets on two or more occasions  
3. A positive result when screening the patient for HLA class I antibodies.
A search is performed on all blood donors suitable to donate apheresis platelets who have been HLA class I typed (and HPA typed where relevant). If compatible HLA/HPA platelets are required, the H&I laboratory and the BTS/Haematology duty specialist registrar should be informed and given as much notice as possible. It takes time to call specific donors in and perform mandatory donor testing before platelets can be released. To monitor the efficacy of HLA/HPA matched platelets, platelet increments should be taken 1 to 24 hours post-transfusion. The increment should be recorded on the NATF1004 form accompanying the matched platelet and returned to the Edinburgh H&I laboratory.
Section IV

H&I Service to Aid Disease Diagnosis

HLA typing can provide help in the diagnosis of various disorders. These tests may be requested by GPs or hospital physicians.

- **HLA-B27 testing to aid diagnosis of ankylosing spondylitis and related spondyloarthropathies.**
  The laboratory will test for the presence of HLA-B27 and report results as positive or negative.

- **HLA-DQB1*06:02 testing to aid with the diagnosis of narcolepsy.**
  HLA-DQB1 testing is performed and the results reported as positive or negative.

- **HLA*DQB1*02 (DQ2) and DQB1*03:02 (DQ8) testing to aid diagnosis of Coeliac disease.**
  HLA-DQB1 and HLA-DQA1 typing is performed and the results reported as positive or negative.

- **HLA-B*57:01 testing is performed to identify individuals who are at risk of hypersensitivity to the anti-HIV drug, Abacavir.**
  The laboratory will test for the presence of HLA-B*57:01 and report results as positive or negative.

- **Other HLA typing tests will be undertaken when referred from a recognised authority and where there is clinical evidence to support HLA typing as providing a useful parameter in diagnosis and/or patient treatment.**

Samples Required: **5ml EDTA** for HLA typing
### Appendix 1

**H&I and Platelet Immunohaematology Laboratory Request Form**

**Solid organ transplant (including islets)**

- **Initial / confirmatory HLA type:**
  - 5ml EDTA

- **HLA antibody screen (inc DSA investigation):**
  - 10ml clotted

- **Initial (Virtual) crossmatch:**
  - 10ml EDTA (donor)
  - 10ml EDTA and 10ml clotted (recipient)

- **Final 'wet' crossmatch**: (by prior arrangement only)
  - 40ml EDTA (donor)
  - 40ml EDTA and 10ml clotted (recipient)

**Platelet refractoriness / FNAIT**

**ALL SAMPLES MUST BE HANDWRITTEN**

- All tests must be arranged via BTS duty haematologist (Daytime 0215 / OOH switchboard 0131 242 1000)

- **Platelet refractoriness:**
  - 5ml EDTA + 10ml clotted (HLA/HPA type and antibody investigation)

- **FNAIT investigations:** (also complete FNAIT form available on NHS Lothian intranet)
  - 5ml EDTA + 10ml clotted (HLA/HPA type and antibody investigation)

**Disease association testing**

**ALL 5ml EDTA**

- HLA B27
- Narcolepsy
- Coeliac
- HLA B*57:01
- Other – please specify

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**Patient / donor information**

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**“Samples must be labelled with the patient’s full name, DoB and CHI number – an alternative unique identifier (hospital number or emergency number) may be used if the patient does not have a CHI number.”**

**Requesting clinician:**

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<th>Routine / urgent*</th>
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<tr>
<th>Risk of infection:</th>
<th>Yes/No</th>
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*Please complete one request form for donor and one for recipient

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**Lab use only**

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